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(54) METHODE POUR MODIFIER LES CONCENTRATIONS D'HOMOCYSTEINE DANS LE PLASMA HUMAIN
(54) METHOD OF ALTERING PLASMA HOMOCYSTEINE LEVELS IN HUMANS

(57)

Plasma homocysteine values > 10.2 .mu.mol per litre are associated with an increased risk of atherothrombosis, but normal values are considered to be 4 to 15 .mu.mol per litre. An initial test subject with Hyper-homocystinemia and lactose intolerance was treated with Sublimed Sulfur 300 mg orally twice daily for 45 days. An additional 46 randomly selected subjects were treated with Sublimed Sulfur 200 mg orally daily for 30 days. Basal control plasma homocysteine, erythrocyte folic acid and serum vitamin B12 and lipids were compared with follow-up results obtained 24 hours and 30 days after discontinuation of Sublimed Sulfur. In the initial test subject, basal plasma homocysteine of 77 .mu.mol per litre decreased by 95.7 percent. In the 46 patients, the effect of Sublimed Sulfur varied according to the initial basal plasma homocysteine concentration; basal levels of 2.3 to 7 .mu.mol per litre increased by 58.5 percent ($p < 0.001$) 24 hours after discontinuation of treatment, and by 85.4 percent 30 days later; basal levels of 7.1 to 9.9 .mu.mol per litre showed no consistent changes, and basal levels of 9.9 to 22.1 .mu.mol per litre decreased to 63.9 percent ($p < 0.005$) of basal levels 24 hours after discontinuation of Sublimed Sulfur, and to 70.7 percent of basal levels 30 days later. Sublimed Sulfur therapy eliminated the initial plasma homocysteine differences between low, intermediate and high basal levels. Sublimed Sulfur therapy normalized plasma homocysteine by causing a regression towards the mean of basal plasma homocysteine levels.

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METHOD OF ALTERING PLASMA HOMOCYST(E)INE LEVELS IN HUMANS

ABSTRACT

Background Plasma homocysteine values > 10.2 μmol per litre are associated with an increased risk of atherothrombosis, but normal values are considered to be 4 to 15 μmol per litre.

Methods An initial test subject with Hyper-homocystinemia and lactose intolerance was treated with Sublimed Sulfur 300 mg orally twice daily for 45 days. An additional 46 randomly selected subjects were treated with Sublimed Sulfur 200 mg orally daily for 30 days. Basal control plasma homocysteine, erythrocyte folic acid and serum vitamin B12 and lipids were compared with follow-up results obtained 24 hours and 30 days after discontinuation of Sublimed Sulfur.

Results In the initial test subject, basal plasma homocysteine of 77 μmol per litre decreased by 95.7 percent. In the 46 patients, the effect of Sublimed Sulfur varied according to the initial basal plasma homocysteine concentration; basal levels of 2.3 to 7 μmol per litre increased by 58.5 percent ($p < 0.001$) 24 hours after discontinuation of treatment, and by 85.4 percent 30 days later; basal levels of 7.1 to 9.9 μmol per litre showed no consistent changes, and basal levels of 9.9 to 22.1 μmol per litre decreased to 63.9 percent ($p < 0.005$) of basal levels 24 hours after discontinuation of Sublimed Sulfur, and to 70.7 percent of basal levels 30 days later. Sublimed Sulfur therapy eliminated the initial plasma homocysteine differences between low, intermediate and high basal levels.

Conclusions Sublimed Sulfur therapy normalized plasma homocysteine by causing a regression towards the mean of basal plasma homocysteine levels.

METHOD OF ALTERING PLASMA HOMOCYST(E)INE LEVELS IN HUMANS

DESCRIPTION

Background Hyper-homocysteinemia is a risk factor for venous thrombosis and atherothrombosis of the coronary, carotid, cerebral, central and peripheral arteries.[1-13] Elevated plasma homocysteine concentrations have been reported in chronic renal failure,[14-15] hypothyroidism, pernicious anemia,[16] advancing age and several types of carcinoma, including breast, ovarian and pancreatic,[17] and in deficiencies of vitamin B12, folic acid,[18-19] vitamin B6,[20] methionine synthase and cystathionine-Beta-synthase.[21] The complications due to atherothrombosis are reported to be associated with plasma homocysteine concentrations > 10.2 μmol per litre[22] but the normal laboratory values are considered to be 4 to 15 μmol per litre.[23] The apparent contradiction between plasma homocysteine concentrations reported to be normal and the values associated with an increased risk of atherothrombosis suggested that one or more additional factors may be necessary for alteration of plasma homocysteine concentrations. Elemental sulfur, an integral component of the sulfur-containing essential amino acids and sulfur-containing enzymes, was considered to be a possible necessary factor, and a clinical study was undertaken to determine the effect of orally administered elemental Sulfur on the Sulfur -containing essential amino acid, homocysteine. Orally administered Sublimed Sulfur USP, and also precipitated sulfur, has been mixed with molasses and used as a laxative.[24-26]

Methods An initial test subject with hyper-homocysteinemia of 77 μmol per litre was treated with Sublimed Sulfur. An additional 46 subjects, 31 men and 15 women were randomly selected. The subjects had single or multiple diagnoses of generalized atherosclerosis, hypertension, myocardial infarction, angina pectoris, peripheral vascular disease, coronary angioplasty, diabetes mellitus, hyperlipidemia, hypothyroidism, past history of carcinoma, hiatus hernia, osteoarthritis and osteoporosis, depression, obstructive airways disease, bronchial asthma, essential tremour, hiatus hernia and the postmenopausal state. A 30 day course of Sublimed Sulfur 200 mg, 1 capsule orally pc breakfast daily, was added to existing medical therapy which was continued unchanged for the duration of the study. Each subject's basal plasma homocysteine was compared with results obtained 24 hours and 30 days after discontinuation of Sublimed Sulfur. Basal and follow-up comparisons were also made for erythrocyte folic acid and serum levels of vitamin B12 and lipids. The subjects did not receive betaine, vitamin B12, folic acid and vitamin B6 during the course of the study.

The Wilcoxon T test was used to evaluate the quantitative data. Numerical values indicate the mean and standard error of the mean.

Results The initial test subject's basal plasma homocysteine of 77 μmol per litre decreased by 95.7 percent. In the 46 additional subjects, the effect of the

Sublimed Sulfur varied according to the initial basal plasma homocysteine concentration; low basal plasma homocysteine levels generally increased and high basal plasma homocysteine levels usually decreased after completion of the 30 day course of Sublimed Sulfur; basal levels of 2.3 to 7 μmol per litre (N=15) increased by 58.5 percent (P<0.001) 24 hours after discontinuation of treatment, and by 85.4 percent 30 days later; basal levels of 7.1 to 9.9 μmol per litre (N=15) showed no consistent changes, and the basal levels of 9.9 to 22.1 μmol per litre (N= 16) decreased to 63.9 percent (P <0.005) 24 hours after discontinuation of Sublimed Sulfur, and to 70.7 percent of basal levels 30 days later.

There were no adverse effects on the pulse rate and rhythm, blood pressure and electrocardiograms. There were no significant changes of the complete blood count, urinalysis, erythrocyte folic acid and serum levels of vitamin B12, creatinine, electrolytes, uric acid, glucose, aspartate transaminase, total cholesterol, high-density lipoprotein cholesterol, triglycerides, and calculated levels of low-density lipoprotein cholesterol and total cholesterol/high-density lipoprotein cholesterol ratio. There were no reports of adverse effects by the subjects.

Conclusions Sublimed Sulfur therapy caused a regression towards the mean of basal plasma homocysteine levels and normalized plasma homocysteine to between 7.5 and 8.5 μmol per litre in subjects with normal levels of erythrocyte

folic acid and serum vitamin B12. Sublimed Sulfur is an effective treatment for the alteration of plasma homocysteine in medical conditions associated with abnormal plasma homocysteine levels.

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CLAIMS

1. A regimen of treatment with Sublimed Sulfur alters plasma homocysteine levels.

2. Treatment with Sublimed Sulfur as defined in claim 1 increases low levels of plasma homocysteine and decreases high levels of plasma homocysteine.

3. Treatment with Sublimed Sulfur as defined in claim 1 and claim 2 causes plasma homocysteine levels to be maintained within the normal range.

4. Sublimed Sulfur alters plasma homocysteine levels as defined in Claim 1, Claim 2 and Claim 3 when administered together with

folic acid,
folic acid and vitamin B6 (pyridoxine),
vitamin B12 (cyanocobalamin) and vitamin B6 (pyridoxine),
vitamin B12 (cyanocobalamin) and folic acid,
vitamin B12 (cyanocobalamin), folic acid and vitamin B6 (pyridoxine),
multi-vitamins,
and foods.

5. Treatment with Sublimed Sulfur as defined in claim 1, claim 2, claim 3 and claim 4 normalizes plasma homocysteine concentrations in

generalized atherosclerosis,
accelerated atherosclerosis,
atherothrombosis,
coronary atherosclerosis,
ischemic heart disease,
angina pectoris,
coronary thrombosis,
myocardial infarction,
atrial arrhythmias,
ventricular arrhythmias,
cardiac nerve degeneration due to atherosclerosis,
carotid atherosclerosis,
recurrent cerebral embolisation,
cerebral atherosclerosis,

transient ischemic attacks,
stroke,
atherosclerotic cerebral degeneration,
peripheral atherosclerosis,
peripheral ischemia,
nerve degeneration due to atherosclerosis in peripheral ischemic neuropathy,
hypertension secondary to generalized atherosclerosis,
atherosclerotic complications of diabetes mellitus,
nerve degeneration due to atherosclerosis in diabetic neuropathy,
recurrent thromboembolism,
deep vein thrombosis and pulmonary embolism,
recurrent pulmonary embolism,
venous thrombosis in cancer,
gout,
Alzheimer's disease,
nephrosclerosis,
chronic renal failure,
menopause,
hypothyroidism,
pernicious anemia,
psoriasis,
leukemias,
cancer,
breast cancer,
ovarian cancer,
pancreatic cancer,
osteoporosis due to atherosclerosis,
and the aging process due to atherosclerosis.